=> s 113

SAMPLE SEARCH INITIATED 13:19:10 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED - 255 TO ITERATE

255 ITERATIONS 100.0% PROCESSED 4 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE** BATCH **COMPLETE** PROJECTED ITERATIONS: 4142 TO 6058 PROJECTED ANSWERS: 4 TO 200

4 SEA SSS SAM L13 L14

=> s 113 sss full

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SEARCH TIME: 00.00.01

L15 44 SEA SSS FUL L13

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=> s 115

L16 1 L15 => d 116 bib abs hitstr L16 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN 2005:570814 CAPLUS DN 143:97397 Preparation of tricyclic 1-[(3-indol-3-yl)carbonyl]piperazine derivatives ΤI as cannabinoid CB1 receptor agonists Adam-Worrall, Julia ΙN PAAkzo Nobel N. V., Neth. SO PCT Int. Appl., 34 pp. CODEN: PIXXD2 DT Patent English LA FAN.CNT 1 KIND DATE APPLICATION NO. PATENT NO. DATE -----_____ ----______ WO 2005058327 20050630 WO 2004-EP53421 PΙ A1 20041213 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG 20041213 AU 2004298782 20050630 AU 2004-298782 A 1 20050630 CA 2004-2549147 CA 2549147 Α1 20041213 EP 1696930 Α1 20060906 EP 2004-804784 20041213 EP 1696930 В1 20070411 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS CN 1893953 20070110 CN 2004-80037747 20041213 Α BR 2004017626 20070327 BR 2004-17626 20041213 Α AT 359078 Τ 20070515 AT 2004-804784 20041213 T T3 JP 2007526242 20070913 JP 2006-544422 20041213 ES 2284076 T3
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PRAI EP 2003-104768 A 20071101 ES 2004-4804784 20041213 20070419 US 2006-583013 20060615 MX 2006-PA6928 20060904 20060616 20031217 Р US 2003-530528P 20031217

WO 2004-EP53421 W 20041213 CASREACT 143:97397; MARPAT 143:97397

Page 2

OS GI

AΒ Tricyclic 1-[(indol-3-yl)carbonyl]piperazine derivs. [X = CH2, O, S; R = 1-3 substituents H, C1-4 alkyl, C1-4 alkyloxy, halo; R1 = C5-8 cycloalkyl; R2 = H, C1-4 alkyl; R3-R6, R13-R16 = H, (un)substituted C1-4 alkyl; ,with (C1-4)alkyloxy, OH or halo; R6R7 may form 4-7 membered saturated heterocyclic ring, optionally containing further heteroatom O and S; R7 = H, (un) substituted C1-4 alky1, C3-5 cycloalky1] or pharmaceutically acceptable salt thereof are described as cannabinoid CB1 receptor agonists. The invention also relates to pharmaceutical compns. comprising I and to their use in the treatment of pain, such as peri-operative pain, chronic pain neuropathic pain, cancer pain, and pain and spasticity associated with multiple sclerosis. Thus, title compound II (as its HCl salt) was prepared in 9 steps from N-tert-butoxycarbonyl-D-cyclohexylglycine, 2-bromophenol, Et pyruvate, and N-ethylpiperazine. II and related compds. I showed pEC50 values between 7.1 and 8.4 at the human cannbinoid CB1 receptor expressed in hamster CHO cells.

IT 856703-13-4P 856703-14-5P 856703-39-4P
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN
 (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
 PREP (Preparation); USES (Uses)

(preparation of tricyclic (indolylcarbonyl)piperazine derivs. as cannabinoid CB1 receptor agonists)

RN 856703-13-4 CAPLUS

CN Piperazine, 1-[(4-cyclopentyl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1-yl)carbonyl]-4-ethyl-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 856703-14-5 CAPLUS

CN Piperazine, 1-[(4-cyclopentyl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1-

yl)carbonyl]-4-methyl-, monohydrochloride, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

HC1

RN 856703-39-4 CAPLUS

CN Piperazine, 1-[(4-cyclopentyl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1-yl)carbonyl]-4-methyl-, monohydrochloride, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

● HCl

IT 856703-38-3P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (preparation of tricyclic (indolylcarbonyl)piperazine derivs. as cannabinoid

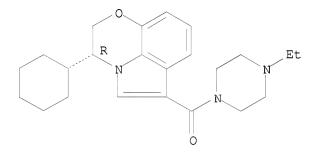
(preparation of tricyclic (indolylcarbonyl)piperazine derivs. as cannabinoid CB1 receptor agonists)

RN 856703-38-3 CAPLUS

CN Piperazine, 1-[[(3R)-3-cyclohexyl-2,3-dihydropyrrolo[1,2,3-de]-1,4-benzoxazin-6-yl]carbonyl]-3,5-dimethyl-, monohydrochloride, (3R,5S)- (9CI) (CA INDEX NAME)

ΙT 856703-03-2P 856703-04-3P 856703-05-4P 856703-06-5P 856703-07-6P 856703-08-7P 856703-09-8P 856703-10-1P 856703-11-2P 856703-12-3P 856703-15-6P 856703-16-7P 856703-17-8P 856703-18-9P 856703-37-2P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of tricyclic (indolylcarbonyl)piperazine derivs. as cannabinoid CB1 receptor agonists) RN 856703-03-2 CAPLUS CN Piperazine, 1-[[(3R)-3-cyclohexyl-2,3-dihydropyrrolo[1,2,3-de]-1,4benzoxazin-6-yl]carbonyl]-4-ethyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



HCl

RN 856703-04-3 CAPLUS
CN 2H-Pyrido[1,2-a]pyrazine, 2-[[(3R)-3-cyclohexyl-2,3-dihydropyrrolo[1,2,3-de]-1,4-benzoxazin-6-yl]carbonyl]octahydro-, monohydrochloride, (9aS)-(9CI) (CA INDEX NAME)

RN 856703-05-4 CAPLUS

CN Piperazine, 1-[[(3S)-3-cyclohexyl-2,3-dihydropyrrolo[1,2,3-de]-1,4-benzoxazin-6-yl]carbonyl]-4-ethyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

● HCl

RN 856703-06-5 CAPLUS

CN Piperazine, 4-[[(3R)-3-cyclohexyl-2,3-dihydropyrrolo[1,2,3-de]-1,4-benzoxazin-6-yl]carbonyl]-1,2-dimethyl-, monohydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 856703-07-6 CAPLUS

CN Piperazine, 1-[[(3R)-3-cyclohexyl-2,3-dihydropyrrolo[1,2,3-de]-1,4-benzoxazin-6-yl]carbonyl]-4-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

● HCl

RN 856703-08-7 CAPLUS

CN Piperazine, 1-[[(3R)-3-cyclohexyl-2,3-dihydropyrrolo[1,2,3-de]-1,4-benzoxazin-6-yl]carbonyl]-2,6-dimethyl-, monohydrochloride, (2R,6S)- (9CI) (CA INDEX NAME)

RN 856703-09-8 CAPLUS

CN Piperazine, 4-[[(3R)-3-cyclohexyl-2,3-dihydropyrrolo[1,2,3-de]-1,4-benzoxazin-6-yl]carbonyl]-1,2,6-trimethyl-, monohydrochloride, (2R,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

● HCl

RN 856703-10-1 CAPLUS

CN Piperazine, 4-[[(3R)-3-cyclohexyl-2,3-dihydropyrrolo[1,2,3-de]-1,4-benzoxazin-6-yl]carbonyl]-1-ethyl-2,6-dimethyl-, monohydrochloride, (2R,6S)- (9CI) (CA INDEX NAME)

HC1

RN 856703-11-2 CAPLUS

CN 1-Piperazineethanol, 4-[[(3R)-3-cyclohexyl-2,3-dihydropyrrolo[1,2,3-de]-1,4-benzoxazin-6-yl]carbonyl]-2,6-dimethyl-, monohydrochloride, (2R,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

● HCl

RN 856703-12-3 CAPLUS

CN Piperazine, 4-[[(3R)-3-cyclohexyl-2,3-dihydropyrrolo[1,2,3-de]-1,4-benzoxazin-6-yl]carbonyl]-1-(2-methoxyethyl)-2,6-dimethyl-, monohydrochloride, (2R,6S)- (9CI) (CA INDEX NAME)

HC1

RN 856703-15-6 CAPLUS

CN Piperazine, 1-[(4-cyclohexyl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1-yl)carbonyl]-4-ethyl-, monohydrochloride, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

● HCl

RN 856703-16-7 CAPLUS

CN Piperazine, 1-[(4-cyclohexyl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1-yl)carbonyl]-4-methyl-, monohydrochloride, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

RN 856703-17-8 CAPLUS

CN Piperazine, 1-[(4-cyclohexyl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1-yl)carbonyl]-4-ethyl-, monohydrochloride, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

● HCl

RN 856703-18-9 CAPLUS

CN Piperazine, 1-[(4-cyclohexyl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-1-yl)carbonyl]-4-methyl-, monohydrochloride, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

RN 856703-37-2 CAPLUS

CN Piperazine, 1-[[(3R)-3-cyclohexyl-2,3-dihydropyrrolo[1,2,3-de]-1,4-benzoxazin-6-yl]carbonyl]-3-methyl-, monohydrochloride, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

● HCl

IT 856703-28-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of tricyclic (indolylcarbonyl)piperazine derivs. as cannabinoid CB1 receptor agonists)

RN 856703-28-1 CAPLUS

CN Piperazine, 1-[[(3R)-3-cyclohexyl-2,3-dihydropyrrolo[1,2,3-de]-1,4-benzoxazin-6-yl]carbonyl]-2,6-dimethyl-4-(phenylmethyl)-, monohydrochloride, (2R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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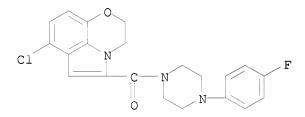
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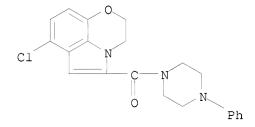
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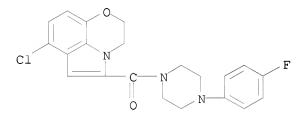
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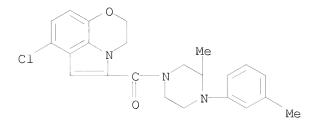
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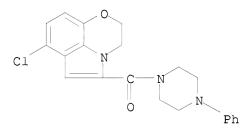
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